IN THE UNTIED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF TENNESSEE WESTERN DIVISION

PATRICIA NOZINICH and PETER NOZINICH,	§	
Plaintiffs',	§	
vs.	§	**Civil Action No.2:09-cv-02105-dkv**
JOHNSON & JOHNSON, INC., and CENTOCOR, INC.,	§	**Jury Demand**
Defendants.	§	

PLAINTIFFS' MEMORANDUM IN SUPPORT OF THEIR MOTION FOR PARTIAL SUMMARY JUDGMENT OR IN THE ALTERNATIVE MOTION TO STRIKE THE LEARNED INTERMEDIARY DEFENSE

The plaintiffs respectfully move the Court to strike any defenses based on the learned intermediary doctrine or assertions that the defendants adequately warned the plaintiffs of risks of pulmonary embolism associated with taking Remicade (Infliximab) because the defendants' warnings were legally sufficient.

INTRODUCTION

A pharmaceutical manufacturer cannot rely on the learned intermediary defense to failure to warn allegations when the pharmaceutical manufacturer directly markets to consumers and fails to provide complete information about the risks of it's product to patients and prescribing physicians. Patricia Nozinich took Remicade to treat rheumatoid arthritis based on the defendants' marketing video and brochures. Dr. Ash,

the physician who prescribed Remicade to Ms. Nozinich, contacted the defendants before prescribing Remicade to Ms. Nozinich to inquire about the risks of thromboembolic events or pulmonary emboli associated with taking Remicade. Dr. Ash was only provided with information on clinical studies and not post-marketing reports showing higher incidents of pulmonary emboli adverse events associated with taking Remicade. Under these facts, should the Court permit the defendants to rely upon the learned intermediary doctrine as a complete defense?

UNDISPUTED, MATERIAL FACTS

A. The defendants used direct to consumer marketing to increase the sales of its drug, Remicade.

Centocor is actively involved in direct to consumer marketing. (Exhibit 1 - CE01886584). In 2000, Centocor invested $17.8 million in direct to consumer marketing for Remicade resulting in a three year annuity value of $216.7 million. (Exhibit 2 - CE00149667). According to Centocor, the 2000 – 2001 revenue generated from direct to consumer marketing was $88.6 million. (Exhibit 2 - CE00149672). In 2001, Centocor considered direct to consumer marketing to be its biggest untapped incremental revenue opportunity to increase the sales of Remicade. (Exhibit 2 - CE00149703)

The defendants had a deliberate plan to market Remicade directly to consumers. (Exhibit 1 - CE01886584). Centocor's key strategic objective of direct to consumer marketing was to "empower patients to demand earlier intervention with Remicade." (Exhibit 1 - CE01886589). Centocor's primary direct to consumer objective is to drive sales by creating doctor/patient conversations so that patients request Remicade. (Exhibit 1 - CE01886589). Centocor's secondary direct to consumer advertising

objective is to collect consumer information, input the information into databases, and market its product by sending the consumers literature on Remicade. (Exhibit 1 - CE01886589).

In 2004, Centocor attributed a 23% increase in its overall rheumatoid arthritis database to direct to consumer marketing. (Exhibit 1 - CE01886607). This direct resulted in 2,899 new patients on Remicade. (Exhibit 1 - CE01886607). In 2004, direct to consumer marketing made Remicade the leader over competitors with a 58% consumer awareness rate. (Exhibit 1 - CE0188660). These 2,899 new patients resulted in $40.6 million of incremental revenue for Centocor. (Exhibit 1 - CE01886607).

Ninety-four percent of Remicade rheumatoid arthritis patients in 2004 said that the Remicade information packet answered all or most of their questions, indicating that patients were more likely to ask their doctor to prescribe Remicade. (Exhibit 1 - CE01886608). Like these patients, Ms. Nozinich relied upon the information presented in the brochure and the DVD when making her decision to treat her rheumatoid arthritis with Remicade. (Exhibit 3 - Nozinich p. 54 and 55).

According to Centocor, direct to consumer marketing has made Remicade the number one requested rheumatoid arthritis therapy. (Exhibit 2 - CE00149671)

B. Ms. Nozinich suffered pulmonary emboli as a result of taking Remicade.

Ms. Nozinich was a patient at the Rheumatology and Osteoporosis Center of Memphis under the care of Dr. Ash from October 1, 2003 to the present. (Exhibit 4 - Ash p. 12). She suffered from rheumatoid arthritis. Ms. Nozinich and Dr. Ash first discussed Remicade in late summer or early fall of 2007 (Exhibit 5 - Nozinich p. 49)

Dr. Ash discussed possible side effects with Ms. Nozinich and gave her a

Remicade brochure entitled "Strong Enough to Change the Course," which included a DVD. (Exhibit 6 - Nozinich p. 51-52) (Exhibit 7 – brochure) (Exhibit 8 - DVD) They did not discuss pulmonary embolism and thromboembolic events as a potential side effect of taking Remicade. (Exhibit 4 - Ash p. 36; Exhibit 6 - Nozinich p. 51-52).

The brochure was produced by Centocor with a copyright date of 2007. (Exhibit 7 - brochure). The brochure was full color and depicted a healthy-looking middle-aged woman jogging on the beach. (Exhibit 7 - brochure). The brochure contained no warning of pulmonary embolism or thromboembolic events. (Exhibit 7 - brochure).

Ms. Nozinich was given a Medication Guide which was included as part of the brochure and a DVD. (Exhibit 9 - Nozinich p. 53). Ms. Nozinich watched the DVD and read the brochure prior to her first infusion on October 30, 2007. (Exhibit 11 - Nozinich p. 54, 57). The Medication Guide provided to her contained no warning of pulmonary embolism or thromboembolic events. (Exhibit 10 - Medication Guide). The DVD depicted multiple patients' experiences while taking Remicade and their positive results. (Exhibit 8 - DVD transcript). The DVD mentions Remicade by name and although a paragraph of "important safety information" scrolls down the screen, the "important safety information" did not include any mention of thromboembolic events or pulmonary embolism. (Exhibit 8 - DVD transcript).

The DVD instructed her to review the medication guide. (Exhibit 8- DVD transcript). The Medication Guide brochure did not contain a warning about thromboembolic events. If the brochure or DVD had warned of pulmonary embolism, Ms. Nozinich would not have taken Remicade. (Exhibit 12 - Nozinich p. 114).

Before her first infusion, Ms. Nozinich was given an informed consent form to

sign prior to receiving the infusion. (Exhibit 13 - Nozinich p. 59). The informed consent form contained no mention of pulmonary embolism. (Exhibit 13 - Nozinich p. 59). After taking Remicade, Ms. Nozinich suffered from multiple and dehibilating pulmonary emboli that were more likely than not caused by taking Remicade. (Exhibit 22 - Trew p. 127)(Exhibit 23 - Expert Disclosure).

C. Dr. Ash inquired about the relationship between thromboemoblic events and Remicade, but Centocor did not provide her with all of the relevant information.

In October 2006, before Dr. Ash considered prescribing Remicade to Ms. Nozinich, she requested information from Centocor on thrombophlebitis (vein inflammation due to a thrombus). (Exhibit 4 - Ash p. 36). Dr. Ash received a response from Centocor listing their clinical trial data which stated that thrombophlebitis and pulmonary embolism were among those things that occurred at a rate equal to placebo. (Exhibit 4 - Ash p. 36). Due to the very low percentage rate given by Centocor in the information provided, Dr. Ash did not consider pulmonary embolism a clinically significant event and did not mention it to Ms. Nozinich in their discussion of side effects of Remicade. (Exhibit 4 - Ash p. 36).

After Ms. Nozinich was hospitalized for pulmonary embolus, Dr. Ash contacted Therese Despeaux, the Centocor sales representative for the Rheumatology and Osteoporosis Center of Memphis, and asked for information regarding Remicade and pulmonary embolism. (Exhibit 4 - Ash p. 37, 40). Dr. Ash was told by Ms. Despeaux that her request would be submitted, and Dr. Ash should receive a letter of response from Centocor. (Exhibit 4 - Ash p. 37). Following her pulmonary embolism, Ms. Nozinich was scheduled to receive another Remicade infusion on February 19, 2008. (Exhibit 4 -

Ash p. 50).

Before administering the February 19, 2008 infusion, Dr. Ash went back and reviewed the information that had been provided to her from Centocor in 2006 regarding thrombophlebitis and pulmonary embolism. (Exhibit 4 - Ash p. 50). Due to the extremely low percentage of risk stated in the report, Dr. Ash determined that Remicade treatment was probably not causative and could be continued. (Exhibit 4 - Ash p. 50)

Dr. Ash received a letter dated February 26, 2008 in response to her second request for information. (Exhibit 14 - Response Letter). The letter contained a 4 page insert entitled "Remicade (Infliximab) Occurrence of Thrombotic Events." (Exhibit 14 - Response Letter). The insert included only clinical data and listed the rate of pulmonary embolism at 0.2% which was equal to the placebo rate. (Exhibit 14 - Response Letter). The insert ended with a statement that a search of available published resources was conducted and resulted in additional reports of thrombotic events, but these cases were not included in the clinical data totals from which the percentage was derived. (Exhibit 14 - Response Letter)

Centocor did not provide Dr. Ash with any additional information or reports other than their initial response letter containing the "Occurrence of Thrombotic Events Insert." (Exhibit 4 - Ash p. 54). Centocor did not provide Dr. Ash with any MedWatch Reports involving pulmonary embolism for her review or evaluation. (Exhibit 4 - Ash p. 54). Centocor did not provide Dr. Ash with any Periodic Safety Update Reports to supplement the clinical data regarding pulmonary embolism. (Exhibit 4 - Ash p. 54).

Dr. Ash would have been open to receiving summaries or Periodic Safety Update Reports and would have considered them in making her determination to

prescribe Remicade for Ms. Nozinich. (Exhibit 4 - Ash p. 55). Dr. Ash stated that any information that can assist in evaluating the care of patients is important to her as a physician. (Exhibit 4 - Ash p. 59).

At the time of Dr. Ash's first request for information regarding thrombotic events, Centocor was in possession of an article regarding an association of increased risk of pulmonary embolism with the use of Infliximab. (Exhibit 15 - CE01569242). This article was submitted to Centocor along with a letter from the SwissMedic regulatory agency requesting comments regarding the 73 identified cases of pulmonary embolism mentioned in the article. (Exhibit 16 - CE01569240 – CE01569241). Neither the article nor information regarding the request from SwissMedic was included in Centocor's response to Dr. Ash's request for information. (Exhibit 14 - Response Letter).

At the time of Dr. Ash's first request for information regarding thrombotic events, Centocor was also in possession of an internal report entitled "Thromboembolic Events during treatment with Infliximab" dated June 1, 2003. (Exhibit 17 - CE00255306 – CE00255313). This report was based on a search of thromboembolic events reported as spontaneous reports, post-marketing studies, literature, registries, and health authority reports in which Infliximab was identified as a suspect or concomitant medication. (Exhibit 17 - CE00255308). The report covered the time period of August 23, 1998 to February 23, 2002 in which 269 cases of thromboembolic events were reported. (Exhibit 17 - CE00255308). Of the 269 cases of thromboembolic events, 109 cases were categorized as pulmonary embolism. (Exhibit 17 - CE00255308). Centocor did not include this report in their response to Dr. Ash's inquiry. (Exhibit 14 - Response Letter).

When Dr. Ash first requested information regarding thrombotic events, Centocor was in possession of a March 25, 2003 database search of MedWatch Reports and CIOMS II Line Listing of Thromboembolic Disorders for Periodic Safety Update Report 7 covering the 6 month period of August 24, 2002 through February 23, 2003 resulting in 121 cases. (Exhibit 18 - CE00246121 – CE00246122) (Exhibit 19 - PSUR 7). 54 of the 121 cases found were categorized as pulmonary embolism. (Exhibit 19 - PSUR 7). Centocor did not include this report in their response to Dr. Ash's inquiry regarding pulmonary embolism and thrombotic events. (Exhibit 14 - Response Letter).

Periodic Safety Update Report 11 covering the period of August 24, 2004 through February 23, 2005 included 69 cases of thromboembolic events, 21 of which were cases of pulmonary embolism. (Exhibit 20 - PSUR 11). Centocor did not include Periodic Safety Update Report 11 in their response to Dr. Ash's inquiry. (Exhibit 14 - Response Letter).

Periodic Safety Update Report 12 covering the period of February 24, 2005 through August 23, 2005 revealed 59 cases of thromboembolic events with pulmonary embolism occurring in 27 of those cases. (Exhibit 21 - PSUR 12). Centocor did not include Periodic Safety Update Report 12 in their response to Dr. Ash's inquiry of thrombotic events. (Exhibit 14 - Response Letter).

SUMMARY JUDGMENT STANDARD

Summary judgment is proper where there is no question of material fact and the moving party is entitled to a judgment as a matter of law. Fed. R. Civ. P. 56(c). A court may grant summary judgment when the inferences arising from the facts demonstrate

that the inferences drawn by the moving party are more plausible. Matushita Elec. Insdutrial Co. v. Zenith Radio Corp, 475 U.S. 574 (1986) (granting summary judgment on conspiracy claim where the facts showed a lack of motive to conspire and thus a reasonable inference from the facts was that no conspiracy existed). The moving party shifts the burden of production to the nonmoving party by demonstrating that the nonmoving party cannot establish an essential element of his claim. Celotex Corporation v. Catrett, 477 U.S. 317, 322–23 (1986). The moving party is not required to negate the nonmoving party's claim to shift the burden of production to the nonmoving party. Id. at 323. Thus, by demonstrating that the nonmoving party lacks evidence supporting an essential element of its claim, the moving party has shifted the burden of production to the nonmoving party to show that a material factual dispute exists. See Id. The Court should construe the evidence in the light most favorable to the nonmoving party and resolve the existence of a genuine issue of material fact in favor of the nonmoving party. City Mgmt Co. v. U.S. Chem. Co., 43 F.3d 244, 250 (6th Cir. 1994).

I. The learned intermediary defense does not apply when drug manufacturers market directly to patients.

It is a normal part of the evening news broadcast: the advertisements promoting the benefits of various prescription drugs. The slick ads promise the benefits of a prescription drug and then at the end of the advertisement speed through the negative side effects and warnings for the drug. The commercials often end with an instruction to ask your doctor.

Magazines and newspapers contain similar slick print ads for drugs making

prescription drugs seem like miracle cures for disease and illness. The internet is also used to extol the virtue of prescription drugs, urging patients to ask for more information directly from the company. Then the company send color, glossy brochures and expensively prepared DVDs to convince a patient that she will benefit from the manufacturer's drug.

The defendants in this case capitalized on the power of direct to consumer marketing to increase the sale of their drug, Remicade, which is used to treat rheumatoid arthritis and other auto-immune diseases. Centocor engaged in a deliberate plan to "empower patients to demand earlier intervention with Remicade." (Exhibit 1 - CE01886589). Its primary objective was to drive sales by creating doctor/patient conversations to request Remicade, and its secondary objective was generate qualified leads into massive consumer databases. (CE 01226604). The defendants succeeded in their objectives: in 2000, Centocor invested $17.8 million in direct to consumer marketing which resulted in a three year annuity value of $216.7 million. (CE00149667).

A. By engaging in direct to consumer marketing, drug manufacturers have changed the way that patients and physicians make decisions about how medications are prescribed.

The way in which drug manufacturers sell pharmaceuticals has drastically changed since the learned intermediary doctrine was initially developed. Courts have observed the drastic shift in the way that health care is delivered and the changes in the relationships among drug makers, physicians and patients. Perez v. Wyeth Laboratories Inc., 734 A.2d 1245, 1251–1253 (NJ 1999); Centocor Inc. v. Hamilton, 310 S.W.3d 476, 507 (Texas Ct. App. 2010). The delivery of health care used to be

physician-patient centric, but

> [o]ur medical-legal jurisprudence is based on the images of health care that no longer exist. At an earlier time, medical advice was received in the doctor's office from a physician who most likely made house calls if needed. The patient usually paid a small sum of money to the doctor. Neighborhood pharmacists compounded prescribed medicines. Without being pejorative, it is save to say that the prevailing attitude of law and medicine was that the "doctor knows best." Johnson & Johnson Corp. v. Karl, 647 S.E.2d 899, 908 (W. Va. 2007)(quoting Logan v. Greenwich Hosp. Ass'n, 465 A.2d 294, 299 (Conn. 1983)).

Health care delivery has changed.

> Significant [technological] advances in [medical] treatment have been accompanied by significant increases in the cost of health care. It is estimated that in 1996, Americans spent more than $1 trillion on health care products and services. Health care is the single largest business in the United States, representing 14% of the gross domestic product. Health care expenses comprise the largest single area of non-government spending.
>
> Corresponding with the financial burdens attendant to our modern health care system, a fundamental change has taken place in the way Americans pay for their health care [from individually-funded to third-party-funded health care].... These fundamental changes have drastically altered the delivery of health care services.
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> ....
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> As [pharmaceutical] manufacturers attempt to appropriately position their products in the chain of delivery, new techniques are often employed to supplement traditional marketing efforts which have historically consisted of direct physician education, information provided in medical references, educational seminars, and research grants....
>
> Among the most controversial of the new marketing techniques employed by pharmaceutical manufacturers is direct-to-consumer prescription advertising in a variety of formats and media. Pharmaceutical remedies for varied problems such as allergies, nail fungus, hypertension, hair loss, and depression are placed directly before the consumer in magazines, television, and via the Internet. The utilization of direct consumer marketing raises questions and issues addressing manufacturer liability

> for failure to adequately warn of risks possibly associated with pharmaceutical use. Perez, 734 A.2d at 1252 (quoting Michael C. Allen, Medicine Goes Madison Avenue: An Evaluation of the Effect of Direct to Consumer Pharmaceutical Advertising on the Learned Intermediary Doctrine, 20 Campbell L. Rev. 113, 113–116(1997)(footnotes omitted)).

The changes in direct to consumer marketing were partly precipitated by a change in the FDA regulations permitting drug companies to name both the drug, its purpose, and list only the significant side effects. Food & Drug Admin., Guidance for Industry: Consumer -Directed Broadcast Advertisements (August 1999)(the guides were issued as draft documents in 1997 and became the FDA's final position in 1999). Before the change drug makers were not permitted to identify the product by name. Alix Spiegel, Selling Sickness: How Drug Ads Changed Health Care, All Things Considered, October 13, 2009 (copy attached). By advertising directly to the patient, drug companies could get patients to ask directly for the drug and "pull the drug through the system" by side-stepping the need to advertise directly to doctors. Id. For example, by advertising on televison directly to consumers, the makers of the non-drowsy allergy medication, Seldane, increased sales from $34 million dollars per year to $800 million per year. Id.

The changes in how prescription drugs are marketed and effectiveness of drug makers marketing strategies is evidenced by the amount of money drug makers spend on direct to consumer marketing. From 1996 to 2005 real spending on direct to consumer marketing increased by 330%. Julie M. Donohue, Ph.D., Marisa Cevasco, B.A. and Meredith B. Rosenthal, Ph.D., A Decade of Direct-to-Consumer Advertising of Prescription Drugs, N. Engl. J. Med 2007, 357, 673–681 (2007)(copy attached). In

fact, in 2005, drug makers spent over four billion dollars in direct to consumer marketing. Id. at Table 1.

B. The theory supporting direct to consumer marketing does not apply when a manufacturer markets directly to a patient.

The learned intermediary doctrine is designed to protect drug makers because traditionally physicians, as the prescribers of medications, act as liaisons, and therefore, warnings must be given to the prescribing physician and not the patient. Restatement (Second) of Torts, § 402A comment k (1965). Under the learned intermediary doctrine, drug makers may discharge their duty by "distributing the drugs with proper directions and adequate warnings to those who foreseeably could be injured by the use of their products." Pittman v. Upjohn Co., 890 S.W.2d 425, 429 (Tenn. 1994) (citing Restatement (Second) of Torts, § 402A comment k (1965) (additional citations omitted)). The learned intermediary defense, however "permits drug companies to communicate directly with patients, thus generating demand for the advertised drugs, but it insulates the drug maker from liability to those same patients based upon those communications." Timothy S. Hall, Regulating Direct-to-Consumer Adverstising with Tort Law: Is the Law Finally Catching Up With the Market?, 31 W. New Eng. L. Rev. 333, 343 (2009).

i. The rationale for the learned intermediary doctrine is no longer valid.

As recognized by the Texas Court of Appeals in Centocor v. Hamilton, 310 S.W.3d 476, 508 (Texas Ct. App. 2010), the rationale behind the learned intermediary

doctrine loses its purpose when a pharmaceutical company markets drugs directly to patients. The basis of the learned intermediary defense is that the physician who meets with the patient is in the best position to warn the patient about the drug. A physician can use his knowledge and skill to take into account the propensities of a drug and the succeptibilities of a patient. Perez v. Wyeth Laboratories Inc., 734 A.2d 1245, 1454–55 (NJ 1999) (citing Reyes v. Wyeth Laboratories, Inc., 489 F.2d 1264, 1276 (5th Cir. 1974)). But, where the physician no longer makes the individualized balancing, the rationale supporting direct to consumer marketing is no longer applicable. Id.

ii. The relationships among drug makers, doctors and patients have changed.

The relationships between pharmaceutical companies, physicians and patients have changed, in part because of pharmaceutical companies' decisive choice to market their products directly to patients. First, due to the changes in managed care, the patient-physician relationship has changed. Physicians do not spend the time needed to inform patients of pharmaceutical warnings. Hamilton, 310 S.W.3d at 508 (citing Perez, 734 A.2d at 1255). The changes in the relationship are further magnified by the fact that patients often ask for drugs by name and make the ultimate decision about which drugs they will take, under informed consent principles. Id.

Second, drug manufacturers should not be permitted to have it both ways. That is, they cannot claim on the one hand that only physicians can understand the dangers associated with a drug and that drug manufactures lack effective means to

communicate with patients as an argument in support of the learned intermediary defense. Yet, on the other hand, continue to market directly to consumers and provide limited warnings in their advertisements. Hamilton, 310 S.W.2d at 508 (citing Perez, 734 A.2d at 1256). The argument that drug manufacturers cannot effectively communicate with patients is belied by the fact that drug manufacturers' advertising campaigns "can pay off in close to billions in dividends." Perez, 734 A.2d at 1256.

Third, it does not make sense to allow drug manufacturers to claim that requiring drug makers to provide direct warnings to patients harms the patient physician relationship, because drug makers have already inserted themselves into this relationship. Hamilton, 310 S.W.3d at 508 (citing Perez, 734 A.2d at 1255). Drug makers' advertising comes into the homes and living rooms of patients and encourages patients to ask for a specific drug by name. Drug makers have already purposefully inserted themselves into the patient-physician relationship by "bring[ing] to 'bear all the slick pressure of which Madison Avenue is capable." Perez, 734 A.2d at 1251 (citing Jon D. Hanson & Douglas A. Kysar, Taking Behaviorlism Seriously: Some Evidence of Market Manipulation, 112 Harv. L. Rev. 1420, 1456 (1999)).

C. The Restatement of Torts Third recognizes the direct-to-consumer marketing exception to the learned intermediary doctrine.

The American Law Institute recognized the rationale for the learned intermediary doctrine is diminished as a result of direct to consumer marketing. Comment e to section 6 of the Restatement (Third) of Torts states that:

> Although the learned intermediary rule is generally accepted and a drug manufacturer fulfills its legal obligation to warn by providing adequate warning to the health-care provider, arguments have been advanced that in two other areas courts should consider imposing tort liablity on the drug manufacturers that fail to provide direct warnings to consumers....[When] manufacturers have advertised a prescription drug and its indicated use in the mass media. Governmental regulations require that, when drugs are so advertised, they must be accompanied by appropriate information concerning risk so as to provide balanced advertising. The question ...is whether adequate warnings to the appropriate health-care provider should insulate the manufacturer from tort liability. Restatement (Third) of Torts: Products Liability §6(d) (1997).

After considering the reasoning supporting the use of adequate warnings directly to patients and the basis for retaining the learned intermediary exception, the ALI concluded that it would leave the issue for the courts to decide. Id.

D. Courts have recognized that the learned intermediary doctrine should not apply in all circumstances.

The erosion of the learned intermediary doctrine began before the proliferation of direct to consumer marketing because courts realized early on that when patients did not confer directly with physicians before receiving pharmaceuticals, the application of the defense was illogical. The learned intermediary doctrine does not apply when drugs are used as inoculation vaccines if dispensed in mass to clinics. Davis v. Wyeth Laboratories, Inc., 399 F.2d 121, 131 (9th Cir. 1968). It does not apply to contraceptives because "the healthy, young consumer of oral contraceptives is usually actively involved in the decision to use "the pill," as opposed to other available birth control products, and the prescribing physician is relegated to a relatively passive role." MacDonald v. Ortho Pharmaceutical Corp., 475 N.E.2d 65, 69 (Mass. 1985); Hill v.

Searle Laboratories, a Div. of Searle Pharmaceuticals, Inc., 884 F.2d 1064, 1071 (8th Cir. 1989)(holding learned intermediary did not apply to IUDs). The learned intermediary doctrine is not a defense when a drug maker fosters and encourages the off-label use of a product, does not seek FDA approval for the use, and never warns physicians about the risks associated with the off-label use. Proctor v. Davis, 682 N.E.2d 1203, 1212–16 (Il Ct. App. 1997) cert. denied, 689 N.E.2d 1146 (1997).

Recently, after the proliferation of direct to consumer marketing, Courts have rejected the learned intermediary defense outright. For example, in Hamilton v. Centocor, Inc. the Texas appellate court rejected the application of the learned intermediary defense, despite the fact that Texas had previously adopted the learned intermediary on the grounds that physicians are the best position to warn patients and that it unreasonable to expect drug makers to warn each and every patient that receives drugs prescribed by a physician. Hamilton, 310 S.W.3d at 501 (citing Gravis v. Parke-Davis Co., 502 S.W.2d 863, 869–71 (Tex. Civ. App. Corpus Cristi 1973, writ ref'd n.r.e.)). Subsequently, in 1986 the Texas Supreme Court formally adopted the learned intermediary doctrine. Hamilton, 310 S.W.3d at 501 (citing Alm v. Aluminium Co. of Am., 717 S.W.2d 588, 591–92 (Tex. 1986).

Johnson & Johnson, Centor and Remicade:

Despite Texas' previously strong endorsement of the learned intermediary doctrine, under the facts presented in Hamilton, which involve the same defendants and the direct to consumer marketing of the same drug, albeit for different purposes and resulting in different injuries, the Texas Court of Appeals reversed its position on

learned intermediary. It held that when a pharmaceutical company directly markets to a patient, it must do so without fraudulently misrepresenting the risks associated with its product. Hamilton, 310 S.W.3d at 508. The Hamilton court reasoned that based on the marketing tactics that Centocor used to increase users of Remicade, "the situation is similar to the recognized exceptions to the doctrine, where courts considering the issue have found it was unreasonable for a manufacturer to rely on an intermediary to convey a warning, given that direct advertising and changes in the provision of healthcare impact the doctor's role and promote more active involvement by the patient." Id.

While the final outcome of Centocor v. Hamilton is still pending before the Texas Supreme Court, Texas has taken steps to join ranks with other states such as West Virginia and New Jersey to decline to apply the learned intermediary doctrine as a result of its lack of relevance in light of direct to consumer marketing. Johnson & Johnson Corp. v. Karl, 647 S.E.2d 899 (WV 2007) (holding "because it is the prescription drug manufacturers who benefit financially from the sales of prescription drugs and possess the knowledge regarding potential harms, and the ultimate consumers who bear the significant health risks of using those drugs it is not unreasonable that prescription drug manufacturers should provide appropriate warnings to the ultimate uses of their products."); Perez v. Wyeth Laboratories Inc., 734 A.2d 1245, 1263(NJ 1999)(the learned intermediary doctrine does not confer on pharmaceutical manufacturers a license to mislead or deceive consumers when those manufactures elect to exercise their right to advertise their product directly to such consumers).

II. Tennessee would not apply the learned intermediary doctrine when drug manufacturers engage in direct to consumer marketing.

A. Tennessee's reasoning for adopting the learned intermediary doctrine is not applicable when drug makers engage in direct to consumer marketing.

The leading case in Tennessee on learned intermediary is Pittman v. Upjohn Co., 890 S.W.2d 425, 428 (Tenn. 1994). The learned intermediary doctrine in Tennessee permits makers of unavoidably unsafe products who have a duty to give warnings the right to rely on intermediaries to transmit their warnings and instructions. Pittman, 890 S.W.2d at 428 citing (Restatement (Second) of Torts, § 388 comment n, (1965); Whitehead v. Dycho Co., 775 S.W.2d 593, 598 (Tenn. 1989); Brushwood & Simonsmeier, Drug Information for Patients, 7 J. Legal Med. 279, 284 (1986). The Upjohn Court explained that physicians are intermediaries because they play a pivotal role in the unique system used to distribute prescription drugs. Upjohn, 890 S.W.2d at 428 (citing W. Page Keeton, et al., Prosser and Keeton on the Law of Torts, § 98, at 688 (5th ed. 1984). Tennessee recognized in 1994 that the "manufacturer of an unavoidably unsafe prescription drug can discharge its duty to warn by providing the physician with adequate warnings of the risks associated with use of its drug." Pittman, 890 S.W.2d at 428 (citations omitted).

Pittman is based on the reasoning that physicians are the users of prescription drugs. Pittman, 890 S.W.2d at 430. The Pittman court reasoned that "[w]here a product is marketed solely to professionals experienced in using the product, the manufacturer may rely on the knowledge that a reasonable professional would apply in using the product." Id. (citing Pavlides v. Galveston Yacht Basin, Inc., 727 F.2d 330,

338 (5th Cir. 1984); Tracy v. Merrell Dow Pharmaceuticals, Inc., 569 N.E.2d 875, 878–79 (1991)). Thus, a pharmaceutical manufacturer could rely a physician's professional expertise and good judgment in preparing its warnings and precautions for a drug. See id.

B. Tennessee would adopt direct to consumer marketing as an exception to the learned intermediary defense.

Pittman and its progeny did not take into consideration the onslaught of direct to consumer marketing that pharmaceutical companies would use to market prescription drugs to the end user, the patient. Pittman was decided in 1994, but since that time, the landscape for selling prescription drugs has dramatically changed. For example, as mentioned earlier, spending on direct to consumer marketing has increased from 985 million dollars annually in 1995 to over four billion in 2005. Julie M. Donohue, A Decade of Direct-to-Consumer Advertising of Prescription Drugs, N. Engl. J. Med. 2007; 357, Table 1.

Notably, Tennessee's position on learned intermediary is not absolute. In Pittman, the Tennessee Supreme Court recognized that "where a product is marketed *solely to professionals experienced in using the product*, the manufacturer may rely on the knowledge that a reasonable professional would apply in using the product." Pittman, 890 S.W.2d at 430 (citing Pavlides v. Galveston Yacht Basin, Inc., 727 F.2d 330, 338 (5th Cir. 1984); Tracy v. Merrell Dow Pharmaceuticals, Inc., 569 N.E.2d 875, 878–79 (1991)) (emphasis added). Based on this limiting word "solely," Tennessee courts would be open to recognizing that direct to consumer marketing creates an

exception to the way that Tennessee defines the learned intermediary doctrine.

Additionally, physicians can be learned intermediaries only if they receive adequate warnings from the manufacturer, and the doctrine does not apply if the manufacturer does not provide adequate warnings to the physician. Pittman, 890 S.W.2d at 429 (citing Amore v. G.D. Searle & Co., 748 F.Supp. 845, 850 (S.D. Fla. 1990); Tracy v. Merrell Dow Pharmaceuticals, Inc., 569 N.E. 2d 875, 878 (Ohio 1991)). Thus, where a party can demonstrate that a physician did not receive an adequate warning, which is defined as full and complete disclosure of the potential adverse reactions to the drug that conveys a fair indication of the dangers involved and the degree of intensity of the nature of the risk, learned intermediary is not applicable. Pittman, 890 S.W.2d at 429.

Based the limitations that Tennessee has already recognized to the learned intermediary doctrine, it is reasonable to conclude, with the proliferation of direct to consumer marketing and the changes in the delivery of healthcare, Tennessee courts would hold that direct to consumer marketing is an exception to the learned intermediary doctrine.

III. The material, undisputed facts show that the Court should not permit the defendants to rely on the learned intermediary defense.

The Court should preclude the defendants from relying on the learned intermediary defense for two reasons. First, the material, undisputed facts show that the defendants intentionally through their DVD and brochure influenced Ms. Nozinich to

take Remicade and that the decision to market directly to patients was made in an effort to maximize the defendants' profits without regard to patient safety. Second, the material, undisputed facts show that the defendants did not provide Dr. Ash with adequate and complete warnings about the association between Remicade and thromboembolic events, specifically pulmonary emboli, and as a result, she could not act as a learned intermediary.

A. The defendants' direct to consumer marketing DVD and brochure convinced Ms. Nozinich to take Remicade, but the information the defendants provided in the material was insufficient to allow her to make an informed choice.

Ms. Nozinich decided to proceed with the Remicade infusion in part because the defendants' marketing materials did not include a warning about thromboembolic events. Ms. Nozinich, who was suffering from rheumatoid arthritis, watched the defendant's DVD, entitled "Strong Enough to Change the Course and read their brochure. (Nozinich p. 54, 57). After doing so, she decided to proceed with Remicade infusions. She was not aware that Remicade was associated with an increased risk of deadly pulmonary emboli or thromboemolic events. Had she been warned of the risks of pulmonary emboli, Ms. Nozinich would not have taken Remicade. (Nozinich p. 114). As a result of taking Remicade, Ms. Noznich suffered multiple, debilitating pulmonary emboli. (Exhibit 22 - Trew p. 127).

What Ms. Nozinich was told about Remicade was how it could help her. (Exhibit 8). She was told by four unpaid patients about how Remicade had transformed their lives and improved their rheumatoid arthritis (RA) symptoms. (Exhibit 8). She was also

told more RA patients take Remicade than any other drug. She was warned about some risks and side effects, but she was never warned of the risk of pulmonary emboli. (Exhibit 8).

Ultimately it was Ms. Nozinich's decision whether she would take Remicade to treat her RA and because the defendants sought to influence her with incomplete information, the defendants should not be permitted to rely on the learned intermediary doctrine to avoid liability for Ms. Nozinich's failure to warn claims. The defendants sought to communicate directly with Ms. Nozinich through their video and brochures. In doing so, they owed her a duty to outline all risks associated with Remicade, not just some of them. They instructed her to review the medication guide, but it did not include any information about pulmonary embolism or thromboembolic events. Accordingly, the warnings they did provide were insufficient. The defendants did not market solely to Dr. Ash. See Pittman, 890 S.W.2d at 430 (citing Pavlides v. Galveston Yacht Basin, Inc., 727 F.2d 330, 338 (5th Cir. 1984); Tracy v. Merrell Dow Pharmaceuticals, Inc., 569 N.E.2d 875, 878–79 (1991)). In seeking to increase sales by marketing directly to consumers like Ms. Noznich, the defendants have taken the physician out the decision, and should not be permitted to rely on the learned intermediary doctrine to avoid responsibility for their conduct. See id.

B. The defendants cannot rely on the learned intermediary doctrine because they did not provide adequate warnings to Dr. Ash.

The material, undisputed facts show that Dr. Ash, before treating Ms. Nozinich, was concerned about the link between Remicade and thrombophlebitis or vein

inflamation that is caused by thrombi (blood clots). (Exhibit 4 p. 36). She requested information regarding this potential side effect. (Id.). What she received in response from the defendants was their clinical trial data stating that thrombophlebitis and pulmonary embolism were among the events that occurred at rate equal to a placebo. (Exhibit 4 p. 36). Based on this information, Dr. Ash concluded that pulmonary embolism was not a clinically siginficant event, and she did not discuss it with her subsequent patient, Ms. Nozinich. (Exhibit 4- p. 36).

This information, however, was not complete. The defendants did not provide Dr. Ash with the following post-clinical trial reports of pulmonary embolism associated with taking Remicade:

- Centocor did not provide Dr. Ash with any MedWatch Reports involving pulmonary embolism for her review or evaluation. (Exhibit 4 - Ash p. 54).
- Centocor did not provide Dr. Ash with any Periodic Safety Update Reports to supplement the clinical data regarding pulmonary embolism. (Exhibit 4 - Ash p. 54).
- At the time of Dr. Ash's first request for information regarding thrombotic events, Centocor was in possession of an article regarding an association of increased risk of pulmonary embolism with the use of Infliximab. (Exhibit 15 - CE01569242).
- Centocor did not provide Dr. Ash with an article regarding an association of increased risk of pulmonary embolism with the use of Infliximab, which had been submitted to Centocor along with a letter from the SwissMedic regulatory agency requesting comments regarding the 73 identified cases of pulmonary embolism mentioned in the article. (Exhibit 16 - CE01569240 – CE01569241).
- Centocor did not provide Dr. Ash with its internal report entitled "Thromboembolic Events During Treatment with Infliximab." This report was based on a search of thromboembolic events reported as spontaneous reports, post-marketing studies, literature, registries, and health authority reports in which Infliximab was identified as a suspect or concomitant medication. (Exhibit 17 - CE00255308).
- The report covered the time period of August 23, 1998 to February 23, 2002 in which 269 cases of thromboembolic events were reported. (Exhibit 17 - CE00255308) Of the 269 cases of thromboembolic events, 109 cases were

categorized as pulmonary embolism. (Exhibit 17 - CE00255308).

- Centocor did not notify Dr. Ash of a March 25, 2003 database search of MedWatch Reports and CIOMS II Line Listing of Thromboembolic Disorders for Periodic Safety Update Report 7 covering the 6 month period of August 24, 2002 through February 23, 2003 showing 121 cases. (Exhibit 18 - CE00246121 – CE00246122) (Exhibit 19 - PSUR 7). 54 of the 121 cases in this report found were categorized as pulmonary embolism. (Exhibit 19 - PSUR 7).
- Centocor did not provide Dr. Ash with Periodic Safety Update Report 11 covering the period of August 24, 2004 through February 23, 2005 including 69 cases of thromboembolic events, 21 of which were cases of pulmonary embolism. (Exhibit 20 - PSUR 11).
- Centocor did not provide Dr. Ash with Periodic Safety Update Report 12 covering the period of February 24, 2005 through August 23, 2005 revealed 59 cases of thromboembolic events with pulmonary embolism occurring in 27 of those cases. (Exhibit 21 - PSUR 12).

Based on the information the defendants withheld from Dr. Ash when she inquired about the connection between Remicade and thromboembolic events, Dr. Ash was not given adequate warnings. For the learned intermediary doctrine to apply under Tennessee law, a warning must "contain a full and complete disclosure of the potential adverse reactions to the drug." Pittman, 890 S.W.2d at 429 (citing Amore v. G.D. Searle & Co., 748 F.Supp. 845, 850 (S.D. Fla. 1990); Tracy v. Merrell Dow Pharmaceuticals, Inc., 569 N.E. 2d 875, 878 (Ohio 1991)). Here, Dr. Ash attempted to determine whether pulmonary embolism was an adverse reaction, but because the defendants withheld relevant and pertinent information, she was unable to make an informed decision about prescribing Remicade. Accordingly, the defendants should not be permitted to hide behind her expertise.

CONCLUSION

The delivery of health care has changed in part because drug makers have sought to promote their drugs by marketing directly to the end-user, the patient. Where the material, undisputed facts show that Ms. Nozinich, the patient, was targeted by the defendants' multi-million dollar marketing effort and took Remicade without being adequately warned of the potential adverse effects in their direct marketing materials, the defendants should not be permitted to escape liability by claiming it was her physician's duty to inform her of the risks associated with their drug. This is particularly true in this case because Dr. Ash, Ms. Nozinich's prescribing physician, attempted to determine if a link existed between thrombotic events and the defendants' drug, Remicade. She contacted the defendants to request this information, but they limited their response to the results from clinical trials. The defendants did not provide her with additional post-trial evidence that suggested a link between pulmonary embolism and Remicade. With these material, undisputed facts in mind, the Court should prohibit the defendants from raising the learned intermediary defense and grant plaintiffs' motion for summary judgment.

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that he is attorney of record for the plaintiff and that he has served a true and correct copy of the foregoing pleading, via electronic filing, through the U.S. District Court's ECF System to:

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